Paper No. 31

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte GREGORY F. HOLLIS, and
GEORGE E. MARK

Appeal No. 2003-1594
Application No. 08/970,266

ON BRIEF

Before SCHEINER, MILLS, and GREEN, Administrative Patent Judges.

GREEN, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 10-25. Claims 10 and 11 are representative of the subject matter on appeal, and read as follows:

10. A method for expression of a recombinant antibody gene in NS/O cells, comprising:

    (a) transferring a vector into said cells, said vector comprising said recombinant antibody gene and murine immunoglobulin gamma 2A locus-specific DNA sequences for homologous recombination targeting, wherein said recombinant antibody gene comprises a nucleic acid encoding for a recombinant antibody and a promoter transcriptionally coupled to said nucleic acid providing for expression in said NS/O cells;

(b) culturing the said cells under conditions suitable for glutamine synthetase selection and recombinant antibody gene expression.

11. A method for expressing a recombinant gene in a murine host cell comprising the following steps:

a) inserting said recombinant gene into a murine immunoglobulin gamma 2A locus present in said murine host, wherein said recombinant gene comprises a nucleic acid encoding for a recombinant protein and a promoter transcriptionally coupled to said nucleic acid providing for expression in said murine host, provided that said recombinant gene is capable of being expressed is [sic] said murine host, and

b) culturing said host under conditions suitable for expression of said recombinant gene.

The examiner relies upon the following references:

Fell et al. (Fell A)	5,204,244	Apr. 20, 1993
Hollis et al. (Hollis)	WO 95/17516	Jun. 29, 1995

Yuriko Yamawaki-Kataoka et al. (Yamawaki-Kataoka), "The complete nucleotide sequence of mouse immunoglobulin γ2a gene and evolution of heavy chain genes: further evidence for intervening sequence-mediated domain transfer," Nucleic Acids Research, Vol. 9, No. 6, pp. 1365-1381 (1981)

Galfre et al. (Galfre), "Preparation of Monoclonal Antibodies: Strategies and Procedures," Methods in Enzymology, Vol. 73, pp. 3-48 (1981)

Sambrook, Molecular Cloning A Laboratory Manual, 2nd Edition, pp. 16.8-16.15 (1989)

Fell et al. (Fell B), "Homologous recombination in hybridoma cells: Heavy chain chimeric antibody produced by gene targeting," Proc. Natl. Acad. Sci. USA, Vol. 86, pp. 8507-8511(1989)

Claim 13 stands rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time of filing, had possession of the claimed invention. Claim 13 stands

rejected under 35 U.S.C. § 102(b) as being anticipated by Hollis. Finally, claims 10-25 stand rejected under 35 U.S.C. § 103 as being rendered obvious by the combination of Fell A or Fell B as combined with Yamawaki-Kataoka. After careful review of the record and consideration of the issues before us, we reverse all of the rejections of record. Note that in deciding this appeal, we have also considered the issues in related Appeal No. 2003-0847, Application No. 08/744,685.

DISCUSSION

1. 35 U.S.C. § 112, first paragraph (New Matter)

Claim 13 stands rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time of filing, had possession of the claimed invention.

The rejection objects to the reference to the selectable markers xanthene-guanine phosphoribosylttransferase (gpt) and dihydrofolate reductase (dhfr).[1] According to the rejection:

> The specification only provides adequate written description for the specifically recited list of recombinant vectors named pMC1neo, pXT1, pSG5, EBO-pSV2-neo, pBPV-1(8-2), pdBPV-MMT-neo, pRSVgpt, pRSVneo, pSV2-dhfr, pUCtag, and IZD35, and does not indicate that it was intended that (1) these vectors encode neo, dhfr or any antibiotic resistance in general or even if these vectors do, that (2) the coding regions for genes comprising neo, dhfr, or

[1] The rejection as set forth in the Answer also objects to the selectable marker of "antibiotic resistance." That phrase was canceled in the Amendment of 4/12/01, however, and thus our analysis does not extend to the rejection as it relates to that selectable marker.

> antibiotic resistance [gpt] [sic] be removed and shuttled to other vectors.

Examiner's Answer, page 4.

Appellants, pointing to the specification at page 6, lines 20-25, and page 7, lines 1-5, contend that the disclosure as filed "provides written description support for the use of the selectable markers gpt and dhfr by general descriptions of selectable markers, providing examples of vectors containing gpt and dhfr, and noting the presence of gpt and dhfr in different vectors." Appeal Brief, page 6.

Page 6 of the specification states that (emphasis added):

> Specifically designed vectors allow the shuttling of DNA between hosts such as bacteria-yeast or bacteria-animal cells. An appropriately constructed expression vector should contain: an origin of replication for autonomous replication in host cells, selectable markers, a limited number of useful restriction enzyme sites, a potential for high copy number, and active promoters.

The paragraph bridging pages 6 and 7 provides examples of commercially available mammalian expression vectors, wherein gpt and dhfr are among the selectable markers used in those expression vectors.

To satisfy the written description requirement, the disclosure as originally filed must convey with reasonable clarity to those skilled in the art that the inventor was in possession of the invention. See Purdue Pharma L.P. v. Faulding, Inc., 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000).

We find that the disclosure as filed conveys to the skilled artisan that appellants were in possession of the claimed invention, i.e., the use of the gpt and dhfr as selectable markers in vectors other than those specifically listed in

the specification. The disclosure as filed teaches the general use of selectable markers, and also discloses the use of the gpt and dhfr markers, albeit in specifically exemplified vectors.

2. 35 U.S.C. § 102(b)

Claim 13 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Hollis. According to the rejection, "[t]his rejection is made because of the priority date granted to this claim in view of the 112 first paragraph rejection above." Examiner's Answer, page 5. Because the new matter rejection under 35 U.S.C. § 112, first paragraph, has been reversed as discussed above, this rejection is also reversed.

3. 35 U.S.C. § 103(a)

Claims 10-25 stand rejected under 35 U.S.C. § 103 as being rendered obvious by the combination of Fell A or Fell B as combined with Yamawaki-Kataoka.

Fell A is relied upon for teaching homologous recombination in hybridoma cells. Fell B is relied upon for teaching a process for producing chimeric antibodies using novel recombinant vectors. According to the rejection, "[t]he recombinant DNA constructs of the invention can be used to transfect antibody producing cells so that targeted homologous recombination occurs in the transfected cells leading to gene modification and the production of chimeric antibody molecules by the transfected cells." Examiner's Answer, page 6. The rejection acknowledges that both references fail to teach the use of a murine gamma 2A locus.

Yamawaki-Kataoka is cited for teaching the complete nucleotide sequence of mouse immunoglobulin gamma 2A gene. The rejection concludes:

> From the knowledge of the murine immunoglobulin [gamma 2A] gene sequence and the teachings of [Fell A or Fell B] it would have been obvious to one skilled in the art at the time the invention was made to modify the vectors of [Fell A or Fell B] to include the IgG2A sequence [to] [sic] permit locus-specific homologous recombination into the immunoglobulin [gamma 2A] gene locus. The combination of [Fell A or Fell B] with Yamawaki-Kataoka [ ] do not teach the use of NS/O cells but instead [Fell B] use murine hybridoma cells substantially similar to NS/O cells. However, as admitted by the specification applicant's admitted prior art at page 3 of the specification "NS/O" cells Galfre [ ] teach NS/O cells. Therefore it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to apply the teachings of [Fell A or B] to that of Yamawaki-Kataoka [ ] to obtain a method using an expression vector for the expression of recombinant immunoglobulin genes in NS/O cells with the vector named pIgG2A. A person of ordinary skill in the art would have been motivated to produce the claimed method to express immunoglobulin genes of interest.

Id. at 7.

The burden is on the examiner to set forth a prima facie case of obviousness. See In re Alton, 76 F.3d 1168, 1175, 37 USPQ2d 1578, 1581 (Fed. Cir. 1996). With respect to an obviousness rejection based on a combination of references, as the court has stated, "virtually all [inventions] are combinations of old elements." Environmental Designs, Ltd. V. Union Oil Co., 713 693, 698, 218 USPQ 865, 870 (Fed. Cir. 1983); see also Richdel, Inc. v. Sunspool Corp., 714 F.2d 1573, 1579-80, 219 U.S.P.Q. (BNA) 8, 12 (Fed. Cir. 1983) ("Most, if not all, inventions are combinations and mostly of old

elements."). Therefore, an examiner may often find every element of a claimed invention in the prior art. If identification of each claimed element in the prior art were sufficient to negate patentability, very few patents would ever issue. The United States Court of Appeals for the Federal Circuit, our reviewing court, however, has stated that "the best defense against hindsight-based obviousness analysis is the rigorous application of the requirement for a showing of a teaching or motivation to combine the prior art references." Ecolochem, Inc. v. Southern California Edison Co., 227 F.3d 1361, 1371, 56 USPQ2d 1065, 1073 (Fed. Cir. 2000).

The rejection fails to show that one of ordinary skill in the art would have been motivated to target the gamma 2A locus as a site for homologous recombination. Fell A and B teach the expression of recombinant genes by homologous recombination. Yamawaki-Kataoka discloses the complete nucleotide sequence of the murine gamma 2A locus. We can find no teaching or suggestion in those references, nor does the examiner point to one, that would lead one of ordinary skill to target the gamma 2A locus as the site for the

homologous recombination. Thus, the rejection fails to provide motivation to combine Yamawaki-Kataoka with either Fell A or B, and the rejection is reversed.

REVERSED

Toni R. Scheiner	)
Administrative Patent Judge	)
	)
	)
	) BOARD OF PATENT
Demetra J. Mills	)
Administrative Patent Judge	) APPEALS AND
	)
	) INTERFERENCES
	)
Lora M. Green	)
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